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| ART UNIT | PAPER NUMBER |
|---|---|
| 1642 | |

DATE MAILED: 02/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/815,340 | Vogelstein et al |
| **Examiner** | **Art Unit** |
| Karen Canella | 1642 |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3 months* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under ***Ex parte Quayle***, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-18* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *6*
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

## DETAILED ACTION

1. Claims 1-18 are pending and examined on the merits.

### *Claim Rejections - 35 USC § 112*

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 11-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 11-15 are drawn to a method of screening compounds to identify potential anti-cancer agents comprising contacting a test compound with a homozygous securing defective cell line and an isogenic cell line which is Securin-proficient and identifying as a potential anti-cancer agent a compound which preferentially inhibits the growth of the Securin-deficient cell line relative to the Securin-proficient cell line, wherein the ration of inhibition is at least 2:1, 5:1, 10:1, 20:1, and 50:1, respectively.

The MPEP (2163) states "To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., Vas-Cath, Inc. v.Mahurkar, 935 F.2d at 1563, 19 USPQ2d at 1116" and "An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Lockwood v.American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir.1997). However, the instant specification provides no description of a compound or compounds which can actually inhibit the growth of a Securin defective cell line

relative to the Securin-proficient cell line at the levels claimed, therefore, the specification lacks adequate written description for a method of screening for an anti-cancer agent exhibiting the specific ratios of inhibition as claimed.

***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-10, 16 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morales (Oncogene, 2000, Vol. 19, pp. 403-409) and Zur et al (EMBO, 2001 Feb 15, Vol. 20, pp. 792-801) in view of Lengauer et al (Nature, 1998, Vol. 396, pp. 643-649). Claim 1 is drawn to an isolated and purified homozygous Securin defective human cell line. Claims 2-4 specifically embody tumor cell lines, colon cell lines and colon tumor cell lines, respectively. Claim 5 is drawn to a pair of isogenic cell lines in which a first cell line is homozygous Securin-defective and a second cell line is Securin proficient. Claims 6-9 specifically embody tumor cell lines, colon cell lines and colon tumor cell lines, respectively. Claim 10 is drawn to a method of screening

compounds to identify potential anti-cancer agents comprising contacting a test compound with each of the isogenic cell lines of claim 5 and identifying as a potential anti-cancer agent a test compound which preferentially inhibits growth of the first cell line relative to the second cell line. Claim 16 embodies the cell lines growing in culture when contacted with the test compound. Claim 18 embodies killing of the first cell line relative to the second cell line.

Morales et al teach that human PTTG is the same as Securin. Morales et al agree with the prior art which postulates that defective Securin results in aneuploidy which contributes to the tumorigenic phenotype (page 407 first column, third line from bottom to second column third line). Morales et al do not teach a homozygous Securin defective cell line, isogenic cell lines comprising said homozygous cell line, nor a method of screening for compounds which inhibit or kill aneuploid cells relative to normal isogenic cells.

Zur et al teach that a cell line overexpressing a double mutant Securin were defective in chromatid separation. Zur et al do not teach a homozygous Securin defective cell line, isogenic cell lines comprising said homozygous cell line, nor a method of screening for compounds which inhibit or kill aneuploid cells relative to normal isogenic cells.

Lengauer et al teach that chromosomal instability is a major factor in the vast majority of cancers and that this is observed as aneuploidy (page 643, first column, under Alterations in chromosome number). Lengauer et al teach that colorectal cells exhibit chromosomal instability (page 645, second column, under heading Relationship between MIN and CIN and page 646, second column, second paragraph). Lengauer et al teach that in order to test if a specific gene is responsible for chromosomal instability it is necessary to have in hand an immortalized cell line in which the targeted gene has been deleted (page 647, second column, lines 4-18). Lengauer et al further teach that the chromosomal instability of cancer cells may provide a valid therapeutic target and can be expected to be sensitive to particular chemical agents relative to the same cells not exhibiting chromosomal instability (page 648, second column). Lengauer et al do not

specifically teach a pair of isogenic cell lines in which the first cell line is homozygous Securin defective and a second cell line which is Securin-proficient.

It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to make a homozygous Securin-defective colon tumor cell line, or other tumor cell line and to use said cell line in combination with an isogenic cell line for the screening of compounds to identify potential anti-cancer agents which preferentially inhibit or kill the homozygous Securin-defective cell line in contrast to the isogenic non-Securin-defective cell line. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Lengauer et all on necessity of having immortalized cell lines in which the gene purported to be responsible for chromosomal instability is deleted and on further teachings of Lengauer et al on the validity of targeting the cells exhibiting chromosomal instability as potential therapeutic targets for particular chemical agents. Further, although Lengauer et al do not specifically teach a pair of isogenic cell lines in which the first cell line is homozygous Securin defective and a second cell line which is Securin-proficient, Lengauer et al do teach a rigorous criteria necessary for the determination of a gene which would be involved in chromosomal instability due to the number of genes which may be involved in the occurrence of aneuploidy. Therefore, one of skill in the art would use isogenic cell lines in order to minimize any differences between the homozygous Securin defective cell line and the Securin proficient cell line.

6. Claims 1-10 and 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morales et al and Zur et al and Lengauer et al as applied to claims 1-10, 16 and 18 above, and further in view of Fiebig et al (Human Tumor Xenographs in Anticancer Drug Development, 1988). The embodiments of claims 1-10 and 16-18 are put forth in paragraph 5, supra. Claim 17 specifies that the cell lines are in xenographs when contacted with the test compound. Although Morales et al in view of Lengauer et al renders obvious the claimed method as drawn to the

testing of isogenic cell lines for the reasons stated in paragraph 5 supra, neither Morales et al nor Lengauer et al teach a cell line in a xenograph. Fiebig et al teach methods of testing anti-cancer drugs using cell lines in xenographs. It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to test the homozygous securing-defective cell line and the isogenic Securin -proficient cell line in xenographs. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Fiebig et al on the nexus between the ability of a drug to kill or inhibit tumor cells in a transplanted in a xenograph and the ability of the drug to kill or inhibit tumor cells in patients.

***Conclusion***

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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February 6, 2002

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